(4)

CGA 329351
(Ridomil Gold 480 EC, 97-817)

Annex II / Section 3
5.2.4/01

Novartis Agro Benelux B.V.
Crop Protection Sector

15 DEC. 1997

Acute Dermal Irritation/Corrosion Study in the Rabbit

Test No. 943028

CGA 329351 tech.

Report

Study director: Dr. med.vet. 5.1.2.e Woo

Testing facility: Short-term Toxicology
CIBA-GEIGY Limited
4332 Stein / Switzerland

Test Guideline: OECD 404; 92/69/EEC, B.4.

Study completed: May 17, 1994

Sponsor: CIBA-GEIGY Limited
Plant Protection
4002 Basel / Switzerland

This report contains: 14 pages

Certification of GLP and verification of the report

(Certification of Good Laboratory Practice and verification of a complete and unaltered copy of the report by the sponsor)

The Statement of Compliance with Good Laboratory Practice found on page 4, and signed by the Study Director is truthful and accurate. This report as provided by the testing facility is complete and unaltered.

For the Sponsor:

Signature: ..... Date: 16 May 1994

Statement of compliance with Good Laboratory Practice

This study has been performed in compliance with Good Laboratory Practice (GLP) in Switzerland (Verfahren und Grundsaetze der Guten Laborpraxis (GLP) in der Schweiz), Procedures and Principles, March 1986, issued by the Swiss Federal Department of the Interior and the Intercantonal Office for the Control of Medicaments. These procedures are in essence consistent with:

- OECD Principles of Good Laboratory Practice (Council Decision 81/30, adopted on May 12, 1981, and the OECD Recommendation 83/95 concerning the 'Mutual Recognition of Compliance with Good Laboratory Practice', adopted on July 26, 1983).

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 160 (FIFRA); Federal Register, August 17, 1989.

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 792 (TSCA); Federal Register, August 17, 1989.

- Japan Ministry of Agriculture, Forestry and Fisheries, NohSan, Notification No. 3850, Agricultural Production Bureau, August 10, 1984.

Study director: Dr. med.vet. 5.1.2.e Woo

Signature: ..... 5.1.2.e Woo ..... Date: May 17, 1994

Dr. med.vet. 5.1.2.e Woo D.A.B.T
Head Shortterm and Reproduction Toxicology

Signature: .. 5.1.2.e Woo .. Date: May 17, 1994

Reserved page for flagging statements

Quality assurance statement

Test Article: CGA 329351 tech.

Study Title: Acute Dermal Irritation/Corrosion Study in the Rabbit

Test Number: 943028

Study Director: Dr. med.vet. 5.1.2.e Woo

I hereby certify that the following Quality Assurance activities were performed:

QA-Activity	Date performed	Date reported
Facility Inspection	March 23, 1994	April 08, 1994
Protocol Audit	April 18, 1994	April 18, 1994
Final Report Audit	May 05, 1994	May 09, 1994

Quality Assurance Inspector: 5.1.2.e Woo

Signature: ..... Date: May 17, 1994

1. SUMMARY AND CONCLUSION

Under the experimental conditions employed CGA 329351 tech. induced slight erythema reactions when applied to the clipped albino rabbit skin. The reactions were observed only one hour after removing the bandages.

Because the mean values of the recordings 24 to 72 hours after application are scored zero, CGA 329351 tech. can be classified as non-irritant according to Council Directive 67/548/EEC, adapted to technical progress by Commission Directive 93/21/EEC.

2. GENERAL

2.1. Introduction

At the request of the Plant Protection of CIBA-GEIGY Limited, an acute skin irritation/corrosion study in albino rabbits was performed to determine the irritant or corrosive potency of CGA 329351 tech. on the albino rabbit skin.

This test was based on the OECD Guideline No. 404, adopted May 12, 1981, adapted July 17, 1992, by the OECD council, and on Annex V, part B of Council Directive 79/831/EEC (Commission Directive 92/69/EEC of July 31, 1992).

Date of protocol: April 13, 1994

Start of experiment: April 19, 1994

End of experiment: April 22, 1994

Testing facility: CIBA-GEIGY Limited
Short-term Toxicology
4332 Stein / Switzerland

Technical assistant: Mr. S1.2e Wood

2.2. Archives

Archives are located at CIBA-GEIGY Limited, Werk Stein CH-4332 Stein, Switzerland. Raw data, protocol and report will be stored at this location.

2.3. Distribution

Sponsor (Dr. 5.1.2.e Woo)
Archives

3. MATERIALS AND METHODS

3.1. Test Article

Test article:	CGA 329351 tech.
Batch No.:	KGL 4634/6
Purity/Contents:	97.30%
Physical properties:	viscous
Storage conditions:	room temperature
Date of reanalysis:	February, 1998
Safety precautions:	gloves and face masks
Test material received:	March 16, 1994

3.2. Test system

The albino rabbit is the recommended species for skin irritation/corrosion studies.

Animal strain:	New Zealand white rabbits (Chbb:NZW)
Breeder:	Dr. 5.1.2.e Woo GMBH Chemisch-pharmazeutische Fabrik D-7950 Biberach/Riss
Acclimatisation period:	at least 5 days

3.3. Group size and husbandry

The test was performed on 3 male rabbits, checked for normal skin conditions, weighing between 2330 to 2590 g. The animals were housed individually in metal cages, identified by ear tattoo, kept at a constant room temperature of 20±3 °C, at a relative humidity of 30-70 % and on a 12 hours light cycle day.

The rabbits received ad libitum standard rabbit pellet - Nafag No. 814, Gossau, Switzerland - and fresh water. All batches of the diet are assayed for nutritive ingredients and contaminant level by the manufacturer. Analytical results are available at the animal supply office.

The drinking water quality fulfilled the critical parameters in the specifications of the "Schweizerisches Lebensmittelbuch" (Edition 1972). The results of the routine chemical examination of water at source (Grundwasserfassung Stein) as conducted periodically by the water authority (Baudepartement des Kantons Aargau, Abteilung Gewaesserschutz) are available to CIBA-GEIGY Limited, as well as the results of inhouse chemical analysis by the analytical laboratories of the Pharmaceutical Division, CIBA-GEIGY Limited.

The bodyweight was recorded at start and on day 3 of the test.

3.4. Method

An area of at least 36 cm^2 was shaved on both flanks of the animals approximately 24 hours before treatment. A gauze patch (approx. 12-16 cm^2) bearing 0.5 ml of the test article was applied to the right flank of each animal. The skin area exposed directly to the test article was approx. 6 cm^2. A control gauze patch moistened with distilled water was applied to the contralateral flank.

The patches were loosely covered with an aluminum foil (approx. 36 cm^2) and held in place for 4 hours by an adhesive tape (Isoplast, Isoplast AG, CH-5200 Brugg).

The animals were checked daily for systemic symptoms and mortality (only findings reported).

The skin reactions were evaluated 1, 24, 48, and 72 hours after removing the gauze patches according to the OECD scoring system (Appendix 1).

The irritant/corrosive potency of CGA 329351 tech. was classified according to Council Directive 67/548/EEC, adapted to technical progress by Commission Directive 93/21/EEC (Appendix 2).

4. RESULTS

The individual reaction scores of the control and treated flanks are summarised in Table 1, the individual bodyweights in Table 2.

Because no reactions were observed at 24 hours to 72 hours after removing the bandages, the test was ended after the 72 hours evaluation.

According to the EEC classification of the results obtained, CGA 329351 tech. can be classified as non-irritant in albino rabbits.

5. TABLES

TABLE 1

Individual skin reaction scores

	E R Y T H E M A			E D E M A		
animal no.	757/M CF/TF	815/M CF/TF	817/M CF/TF	757/M CF/TF	815/M CF/TF	817/M CF/TF
after 1 hr.	0/0	0/1	0/1	0/0	0/0	0/0
after 24 hrs.	0/0	0/0	0/0	0/0	0/0	0/0
after 48 hrs.	0/0	0/0	0/0	0/0	0/0	0/0
after 72 hrs.	0/0	0/0	0/0	0/0	0/0	0/0
mean 24-72 hrs.	0/0	0/0	0/0	0/0	0/0	0/0

CF = control flank TF = test flank
M = male

TABLE 2

Bodyweights (g)

animal no.	757/M	815/M	817/M
at start of test	2590	2510	2330
after 3 days (end)	2670	2610	2430

6. APPENDICES

APPENDIX 1

OECD guideline No. 404

Erythema and eschar formation

No erythema.....0
Very slight erythema (barely perceptible).....1
Well defined erythema.....2
Moderate to severe erythema.....3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....4

Total possible erythema score.....4

Edema formation

No edema.....0
Very slight edema (barely perceptible).....1
Slight edema (edges of area well defined by definite raising).....2
Moderate edema (raised approximately 1 mm).....3
Severe edema (raised more than 1 mm and extending beyond area of exposure).....4

Total possible edema score.....4

APPENDIX 2

Annex IV, 3.2.6 of Council Directive 67/548/EEC (Commission Directive 93/21/EEC of April 27, 1993; Official Journal of the European Communities No. L 110 A, May 4, 1993)

(a) Corrosion criteria

A substance or a preparation is considered to be corrosive if, when it is applied to healthy intact animal skin, it produces full thickness destruction of skin tissue on at least one animal during the test for skin irritation cited in Annex V or during an equivalent method or if the result can be predicted, for example from strongly acid or alkaline reactions.

(b) Irritation criteria

A substance or a preparation is considered to be irritant if it causes inflammation of the skin corresponding to the evaluation of the parameters given below:

1. Inflammation of the skin

(i) Inflammation of the skin which persists for at least 24 hours after an exposure period of up to four hours and corresponds to the following values determined on the rabbit according to the cutaneous irritation test method cited in Annex V:

- the mean value of the scores for either erythema and eschar formation or edema formation, calculated over all the animals tested, is two or more,

- or, in the case where the Annex V test has been completed using three animals, either erythema and eschar formation or edema formation equivalent to a mean value of two or more calculated for each animal separately has been observed in two or more animals.

In both cases all scores at each of the reading times (24, 48, and 72 hours) for an effect should be used in calculating the respective mean values.
Inflammation of the skin is also significant if it persists in at least two animals at the end of the observation time. Particular effects e.g. hyperplasia, scaling, discolouration, fissures, scabs and alopecia should be taken into account.

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